

IN THE CLAIMS

23. (Currently amended) A bacteria [Bacteria] useful as a vehicle for gene transport and gene transfer to eukaryotic cells of an organism for inducing a targeted somatic transgenesis in cells, tissues or organs, except the germ-line cells of the organism, the bacteria comprising a foreign DNA integrated into an episomal vector, the transcription and expression of the foreign DNA being under the control of a eukaryotic regulator gene selected from the group consisting of a promoter and other regulatory sequence, wherein the bacteria:

- a. are vital and viable in the organism;
- b. have pathogenic properties selected from the group consisting of:
 - a. i. fully pathogenic;
 - b. ii. attenuated in one or more of the following ways:
 - (1) attenuated to prevent the bacteria from inducing apoptosis of the eukaryotic cells,
 - (2) attenuated to restrict the intracellular motility of the bacteria, and
 - (3) attenuated so as to permit efficient elimination of the bacteria after the foreign DNA is transferred to the eukaryotic cells; and
 - iii. naturally not pathogenic bacteria that is provided with additional pathogenicity factors, said factors enabling the bacteria to infect the organism in a controlled manner, to advance into the organs and


tissue of the organism, and to transfer the foreign DNA to remote somatic cells;

- c. reach the target organ in the organism according to their typical cycle of infection and by their typical route of infection and are able to transmit the foreign DNA into remote somatic cells;
- d. have the route of infection that is directed and locally limited either naturally or due to a specific genetic alteration of one or more genes selected from the group consisting of:
- i. genes that influence the reproduction of the bacteria in the eukaryotic cells,
 - ii. genes that reduce the pathogenicity of the bacteria in the organism, and
 - iii. genes that inhibit the survival of the bacteria in the environment after the bacteria is excreted from the organism; and
- e. having the cycle of infection that can be limited in time and terminated by use of an antibiotic.

24. (Currently amended) The bacteria of claim 23, [in which the foreign DNA is controlled by a promoter and other regulatory sequence,] wherein the promoter and other regulatory sequence originate from the previously selected target organ or are optimized from the target organ.

25. (Original) The bacteria of claim 23, wherein the bacteria further comprises an additional exogenous suicide gene.

26. (Original) The bacteria of claim 23, wherein the bacteria belongs to a genus selected from the group consisting of: Aeromonas, Bartonella, Brucella, Campylobacter, Clostridia, Enterobacteriaceae, Legionella, Listeria, Mycobacterium, Renibacterium, Rhodococcus, and a genus that is genetically or biochemically related to them.


 27. (Currently amended) A bacteria useful as a vehicle for gene transport and gene transfer to eukaryotic cells of an organism for inducing a targeted somatic transgenesis in cells, tissues or organs, except the germ-line cells of the organism, the bacteria comprising a foreign DNA integrated into an episomal vector, the transcription and expression of the foreign DNA being under the control of a eukaryotic regulator gene selected from the group consisting of a promoter and other regulatory sequence, wherein the bacteria:

- a. are vital and viable in the organism;
- b. have pathogenic properties selected from the group consisting of:
 - c. i. fully pathogenic;
 - d. ii. attenuated in one or more of the following ways:

(1) attenuated to prevent the bacteria from inducing apoptosis of the eukaryotic cells,

(2) attenuated to restrict the intracellular motility of the bacteria, and

(3) attenuated so as to permit efficient elimination of the bacteria after the foreign DNA is transferred to the eukaryotic cells; and

 iii. naturally not pathogenic bacteria that is provided with additional pathogenicity factors, said factors enabling the bacteria to infect the organism in a controlled manner, to advance into the organs and tissue of the organism, and to transfer the foreign DNA to remote somatic cells;

c. reach the target organ in the organism according to their typical cycle of infection and by their typical route of infection and are able to transmit the foreign DNA into remote somatic cells;

d. have the route of infection that is directed and locally limited either naturally or due to a specific genetic alteration of one or more genes selected from the group consisting of:

i. genes that influence the reproduction of the bacteria in the eukaryotic cells,

ii. genes that reduce the pathogenicity of the bacteria in the organism, and

iii. genes that inhibit the survival of the bacteria in the environment after the bacteria is excreted from the organism; and


- f. having the cycle of infection that can be limited in time and terminated by use of an antibiotic;

[The bacteria of claim 23, in which] wherein the bacteria contains a dapE gene having a nucleotide sequence set forth in SEQ ID NO. 1 or a gene matching in at least [35] 50-60% of the nucleotide positions with the dapE gene, wherein the dapE gene or the matching gene is deleted or inhibited by blocking or mutation.

28. (Original) The bacteria of claim 27, wherein the bacteria is of strain *Listeria monocytogenes*.

29. (Currently amended) A bacteria useful as a vehicle for gene transport and gene transfer to eukaryotic cells of an organism for inducing a targeted somatic transgenesis in cells, tissues or organs, except the germ-line cells of the organism, the bacteria comprising a foreign DNA integrated into an episomal vector, the transcription and expression of the foreign DNA being under the control of a eukaryotic regulator gene selected from the group consisting of a promoter and other regulatory sequence, wherein the bacteria:

- a. are vital and viable in the organism;
- b. have pathogenic properties selected from the group consisting of:
 - e. i. fully pathogenic;
 - f. ii. attenuated in one or more of the following ways:

- (1) attenuated to prevent the bacteria from inducing apoptosis of the eukaryotic cells,
 - (2) attenuated to restrict the intracellular motility of the bacteria, and
 - (3) attenuated so as to permit efficient elimination of the bacteria after the foreign DNA is transferred to the eukaryotic cells; and
- iii. naturally not pathogenic bacteria that is provided with additional pathogenicity factors, said factors enabling the bacteria to infect the organism in a controlled manner, to advance into the organs and tissue of the organism, and to transfer the foreign DNA to remote somatic cells;
-  c. reach the target organ in the organism according to their typical cycle of infection and by their typical route of infection and are able to transmit the foreign DNA into remote somatic cells;
- d. have the route of infection that is directed and locally limited either naturally or due to a specific genetic alteration of one or more genes selected from the group consisting of:
 - i. genes that influence the reproduction of the bacteria in the eukaryotic cells,
 - ii. genes that reduce the pathogenicity of the bacteria in the organism, and

- iii. genes that inhibit the survival of the bacteria in the environment after the bacteria is excreted from the organism; and
- f. having the cycle of infection that can be limited in time and terminated by use of an antibiotic;

[The bacteria of claim 23,] wherein said bacteria containing a cspL gene having a nucleotide sequence set forth in SEQ ID NO 2 or a gene matching in at least [35] 50-60% of the nucleotide positions with the cspL gene, wherein the cspL gene or the matching gene is deleted or inhibited by blocking or mutation.

30. (Original) The bacteria of claim 29, wherein the bacteria belongs to the genus *Listeria*.


31. (Previously amended) A bacterial strain *Listeria monocytogenes* EGD Hyl_{D491A} which is deposited at the DSMZ (German Collection of Microorganisms and Cell Cultures) under the number of 11881 and is suitable for use according to claim 23.

32. (Original) A bacterial strain *Listeria monocytogenes* EGD Delta actA Delta plcB, which is deposited at the DSMZ (German collection of Microorganisms and Cell Cultures) under the number 11882 and is suitable for use according to claim 23.

33. (Original) A bacterial strain *Listeria monocytogenes* EGD Delta cspL 1, which is deposited at the DSMZ (German collection of Microorganisms and Cell Cultures) under the number 11883 and is suitable for use according to claim 22.

34. (Original) The bacteria of claim 23, wherein the bacteria infect udders of cows or other lactating working animals.

35. (Withdrawn) A method for the production and extraction of proteins, comprising:

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- a. providing bacteria useful as a vehicle for gene transport and gene transfer to eukaryotic cells of an organism (a TGC procedure) for inducing a targeted somatic transgenesis in these cells, tissue or organs, except the germ-line cells of the organism, said bacteria comprising a foreign DNA integrated in an episomal vector, the transcription and expression of the foreign DNA being under the control of a eukaryotic regulator gene;
 - b. infecting the eukaryotic somatic cells of the organism with the bacteria to produce transgenic cells, said transgenic cells expressing the foreign DNA to produce a foreign protein encoded by said foreign DNA; and
 - c. isolating the foreign protein from the cell, tissue or organ, wherein the bacteria:
 - i. are vital and viable in the organism;

ii. have pathogenic properties selected from the group consisting of


- (1) fully pathogenic;
- (2) attenuated in one or more of the following ways:
 - (a) attenuated to prevent the bacteria from inducing apoptosis of the eukaryotic cells,
 - (b) attenuated to restrict the intracellular motility of the bacteria, and
 - (c) attenuated so as to permit efficient elimination of the bacteria after the foreign DNA is transferred to the eukaryotic cells; and

(3) naturally not pathogenic bacteria that is provided with additional pathogenicity factors, said factors enabling the bacteria to infect the organism in a controlled manner, to advance into the organs and tissue of the organism, and to transfer the foreign DNA to remote somatic cells;

iii. reach the target organ in the organism according to their typical cycle of infection and by their typical route of infection and are able to transmit the foreign DNA into remote somatic cells;

iv. have the route of infection that is directed and locally limited either naturally or due to a specific genetic alteration of one or more genes selected from the group consisting of

- (1) genes that influence the reproduction of the bacteria in the eukaryotic cells,
 - (2) genes that reduce the pathogenicity of the bacteria in the organism, and
 - (3) genes that inhibit the survival of the bacteria in the environment after the bacteria is excreted from the organism; and
- v. having the cycle of infection that can be limited in time and terminated by use of an antibiotic.




36. (Withdrawn) The method of claim 35, wherein the method further comprises the step of washing the foreign protein isolated from the cell, tissue or organ.

37. (Withdrawn) The method of claim 35, wherein the foreign DNA is controlled by a promoter and other regulatory sequence, wherein the promoter and other regulatory sequence originate from the previously selected target organ or are optimized from the target organ.

38. (Withdrawn) The method of claim 35, wherein the bacteria further comprises an additional exogenous suicide gene.

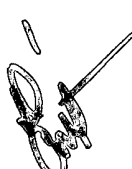
39. (Withdrawn) The method of claim 35, wherein the bacteria belongs to a genus selected from the group consisting of: Aeromonas, Bartonella, Brucella, Campylobacter, Clostridia, Enterobacteriaceae, Legionella, Listeria, Mycobacterium, Renibacterium, Rhodococcus, and a genus that is genetically or biochemically related to them.
40. (Withdrawn) The method of claim 35, wherein the bacteria contains a dapE gene having a nucleotide sequence set forth in SEQ ID NO. 1 or a gene matching in at least 35% of the nucleotide positions with the dapE gene, wherein the dapE gene or the matching gene is deleted or inhibited by blocking or mutation.
41. (Withdrawn) The method of claim 35, wherein the bacteria is of strain *Listeria monocytogenes*.
42. (Withdrawn) The method of claim 35, wherein the bacteria contains a cspL gene having a nucleotide sequence set forth in SEQ ID NO 2 or a gene matching in at least 35% of the nucleotide positions with the cspL gene, wherein the cspL gene or the matching gene is deleted or inhibited by blocking or mutation.
43. (Withdrawn) The method of claim 35, wherein the bacteria belongs to the genus *Listeria*.
44. (Withdrawn) The method of claim 35, wherein the bacteria is of the strain *Listeria monocytogenes* EGH H1yD_{491A}, which is deposited at the DSMZ (German collection of Microorganisms and Cell Cultures) under the number 11881.

45. (Withdrawn) The method of claim 35, wherein the bacteria is of the strain *Listeria monocytogenes* EGD Delta actA Delta plcB, which is deposited at the DSMZ (German collection of Microorganisms and Cell Cultures) under the number of 11882.
46. (Withdrawn) The method of claim 35, wherein the bacteria is of the strain *Listeria monocytogenes* EGD Delta cspL 1, which is deposited at the DSMZ (German collection of Microorganisms and Cell Cultures) under the number of 11883.
-  47. (Withdrawn) The method of claim 35, wherein the organism is selected from the group consisting of: (a) a working animal, with the transgenesis being induced in the blood or other tissue of the working animal, (b) a lactating animal, with the transgenesis being induced in the udder of the lactating animal, and (c) poultry, with the transgenesis being induced in eggs of the poultry.
48. (Withdrawn) A somatic transgenic working animal produced by the method of claim 35.
49. (Withdrawn) The method of claim 35, in which the somatic transgenic tissue created through infection with the bacterium of claim 1 is reimplanted in an entire organism.

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AMENDMENT C

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50. (Withdrawn) The method of claim 35, wherein the foreign protein is selected from the group consisting of hormone, regulation factor, enzyme, enzyme inhibitor and a human monoclonal antibody.



51. (Withdrawn) The method of claim 47, wherein the foreign protein is useful as a drug, vaccine, or for preparation of diagnostics.
